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AMASIA: real world insight into the impact of siponimod treatment on disease progression of SPMS patients in Germany

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CONCLUSIONS

1. **AMASIA provides real-world evidence on the use of siponimod in the treatment of active SPMS patients in Germany.**
2. **On average, cognition and overall health status as reflected by EDSS and SDMT remained stable over 18 months of siponimod treatment regardless of subgroup. UKNDS (patient reported) further confirms the overall stabilization of disease progression.**
3. **Stabilization of disease progression was found to be independent of patients' last therapy before switching to siponimod, including treatment-naive patients.**
4. **Overall, the results indicate stabilization of disease status regardless of subgroup. This underlines the benefit of early initiation of siponimod treatment in patients diagnosed with active SPMS.**

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INTRODUCTION

- 85% of Multiple Sclerosis (MS) patients are initially diagnosed with relapsing-remitting MS (RRMS).[1]
- 60% will convert to secondary progressive MS (SPMS) within 20 years due to evolvement of the disease over time.[2,3]
- In the EU, siponimod, a selective sphingosine-1-phosphate receptor modulator, is approved specifically for the treatment of active SPMS as evidenced by relapses or imaging features of inflammatory activity.
- Randomized controlled trials (RCTs) impose rigid inclusion criteria and assessment schedules for outcome parameters, whereas the general patient population seen in clinical routine is more variable. Thus, data from real world settings are mandatory to complement data obtained from RCTs.

OBJECTIVE

- The non-interventional AMASIA study will provide real-world evidence on the long-term effectiveness and safety of siponimod as well as its impact on quality of life.

METHODS

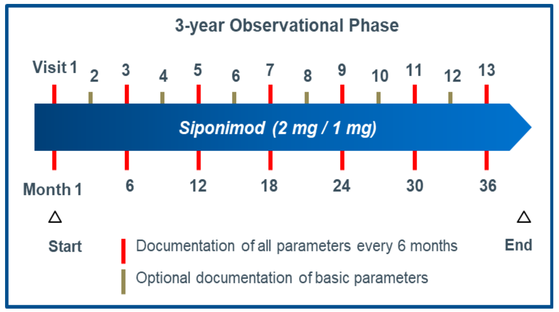
Study Design

- Non-interventional study, observational phase: 2-3 years with study visits every 6 months (Figure 1)
- 673 siponimod-treated SPMS patients with disease activity at 104 sites in Germany out of which 670 patients were available for the analysis

Assessment

- Clinic: Laboratory, ophthalmic, and physical evaluation
- MS-activity: Magnetic Resonance Imaging (MRI), MS Activity Scale Score (MS-AS), Expanded Disability Status Scale (EDSS)
- Functional domains: Symbol Digit Modalities Test (SDMT), EDSS
- Patient's perspective: United Kingdom Neurological Disability Scale (UKNDS), Fatigue Scale For Motor And Cognitive Functions (FSMC), EuroQol-5D (EQ-5D)
- Physician's perspective: Clinical Global Impression (CGI), progression questionnaire
- Socioeconomic factors: Multiple Sclerosis Health Resource Survey (MS-HRS).

Figure 1. Study design.



RESULTS

Study Population

- The baseline data of AMASIA patients after completion of recruitment (cut-off February 9th, 2023) are compared to the active SPMS subgroup population of the pivotal EXPAND RCT (Tab. 1) .
- The real-life population of AMASIA seems older with a longer disease history and a higher proportion of relapses within the 24 months before study start in comparison to the active subgroup of EXPAND.
- The majority of the study population is female (69%) (Fig. 2).
- Before switching to siponimod, about half of all patients (48.2%) had received a moderately effective therapy and nearly one quarter of patients (23.9%) was treated with a highly effective therapy (Fig. 3).
- About 10% of patients were treatment naive at study start (Fig. 3)

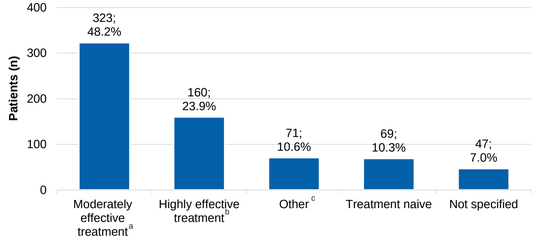
Table 1. Patient characteristics at baseline.

Variable	AMASIA	EXPAND (active SPMS subgroup[a])
Number of patients (n)	670	779
Age, n=670 (years) (± SD)	55±8.4	47
Time since first MS diagnosis, n=633 (years) (± SD)	17.3±9.5	13
EDSS, n=618 (score) (± SD)	5.1±1.5	6
SDMT, n=529 (score) (± SD)	39.7±13.1	38.3
Patients with relapse (past 24 months) (%)	43.1	36

[a] Represents population of EMA label.

Figure 2. Gender distribution at baseline; n=670.

Figure 3. Last therapy before starting siponimod treatment.



[a] Moderately effective treatment: interferons, dimethyl fumarate, teriflunomide, glatiramer acetate. [b] Highly effective treatment: fingolimod, ocrelizumab, natalizumab, cladribine, alemtuzumab. [c] Other: mitoxantron, azathioprine, daclizumab, rituximab.

Disease Progression

- Disease progression (EDSS, SDMT) by subgroups (age, time since diagnosis, EDSS at study start and last pretreatment) was monitored over 18 months.
- At baseline, patients aged 50 years or less (≤50Y) had the same EDSS score as the older patient group (>50Y) but showed a higher (better) SDMT score (Fig. 4a, b).
- Patients who were diagnosed 10 years or less before study start (≤10Y) presented with an overall better health status (EDSS, SDMT) at baseline than to patients who were diagnosed more than 10 years before enrollment (Fig. 5a, b).
- Overall, patients who had an EDSS score of 4 or less at study start (mean EDSS 3.3±0.8) had a higher SDMT score compared to patients who had an EDSS of more than 4 (mean EDSS 6.9±0.8) at baseline (Fig. 6a, b).
- On average, cognitive and general health status as reflected by EDSS and SDMT remained stable over 18 months of siponimod therapy regardless of
  - patient age (Fig. 4a, b),
  - time since MS diagnosis (Fig. 5a, b) and
  - EDSS score at study start (Fig. 6a, b).

Figure 4. a) EDSS and b) SDMT scores of younger (≤50 years) and older (>50 years) patients at baseline (BL) and after 18 months (18M).

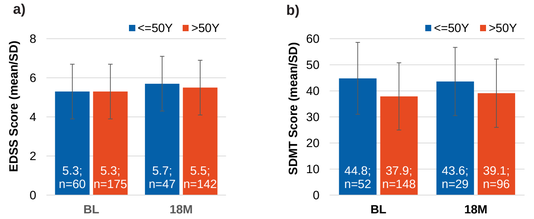


Figure 5. a) EDSS and b) SDMT scores of patients diagnosed with MS ≤10 years and >10 years before study start at baseline (BL) and after 18 months (18M).

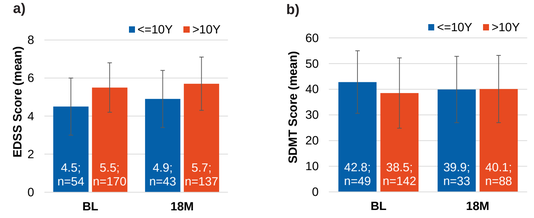
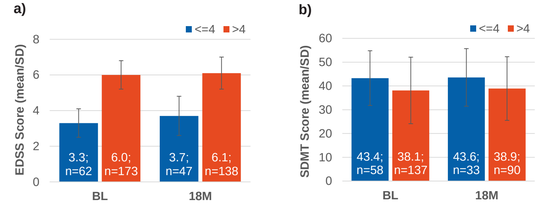
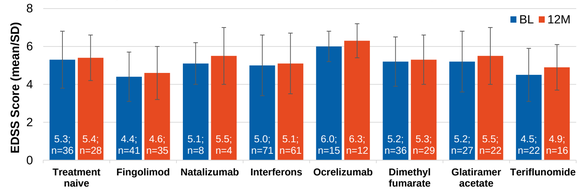


Figure 6. a) EDSS and b) SDMT scores of patients with EDSS ≤4 and EDSS >4 at study start at baseline (BL) and after 18 months (18M).



- On average, documentation of EDSS over 12 months based on last therapy before switching to siponimod (most often reported therapies and treatment-naive) showed stabilization of disease progression independent of pretreatment (Fig. 7).

Figure 7. EDSS at baseline (BL) and after 18 months (18M) depending on last therapy before siponimod (most often named pretreatments[a]).



[a] Percentage of patients on respective last treatments before switching to siponimod: treatment naive 10.3%, fingolimod 12.7%, natalizumab 2.8%, interferons 18.4%, ocrelizumab 5.4%, dimethyl fumarate 12.1%, glatiramer acetate 8.1%, teriflunomide 9.7%.

- Across all patients, UKNDS data show a stabilization of patient reported disease progression over 18 months on siponimod (Fig. 8).
- Quality of life as documented using Visual Analogous Scale (VAS) of EQ-5D remained at a stable level over 18 months (Fig. 9).

Figure 8. UKNDS at baseline (BL) and after 18 months (18M).

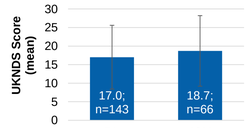
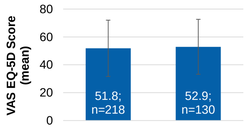


Figure 9. VAS EQ-5D at baseline (BL) and after 18 months (18M).



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